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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/913,538	08/15/2001	Fuminori Sato		9756

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EXAMINER	
LUKTON, DAVID	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 04/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/913,538	SATO ET AL.	
	Examiner	Art Unit	
	David Lukton	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9 and 10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Pursuant to the directives of the response filed 2/12/04, claims 4, 9 and 10 have been amended. Claims 1-7, 9 10 remain pending.

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 10 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As observed previously, claim 10 recites the term "pharmaceutical". This term implies an assertion of therapeutic efficacy, which is not in evidence. The specification (page 2) asserts that any or all of the following diseases can be successfully treated: pulmonary emphysema, adult respiratory distress syndrome (ARDS), idiopathic interstitial pneumonia, cystic pulmonary fibrosis, chronic interstitial pneumonia, chronic bronchitis, chronic sinopulmonary infection, diffuse panbronchiolitis, bronchiectasis, asthma, pancreatitis, nephritis, hepatic failure, chronic rheumatoid arthritis, joint scleroma, osteoarthritis, psoriasis,

periodontitis, atherosclerosis, rejection against organ transplant, premature amniorrhexis, bullous dermatosis, shock, sepsis, systemic lupus erythematosus (SLE), Crohn's disease, disseminated intracapillary coagulation (DIC), tissue injury after ischemia/reperfusion, formation of corneal cicatricial tissue, and myelitis.

In the specification, data is presented which shows that the claimed compounds can inhibit elastase *in vitro*. The examiner will stipulate that inhibition of elastase will occur *in vivo* as well. In addition to the foregoing, an experiment is described (page 23) in which one of the claimed compounds is administered to hamsters, followed by administration of neutrophil elastase; the concentration of hemoglobin in the washing of the broncho-alveolar lavage was subsequently measured. It was found that the amount of hemoglobin in the washing of the broncho-alveolar lavage was reduced if the (claimed) compound was administered, relative to the amount of hemoglobin present if the compound was not administered. Based on these results, it is asserted (in effect) that one or more of the diseases referred to above can be successfully treated. However, it is not clear how one can justify such an extrapolation. As stated in *Ex parte Forman* (230 USPQ 546, 1986) and *In re Wands* (8 USPQ2d 1400, Fed. Cir., 1988) the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of

working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims. As it happens, extrapolation from the two experiments described above to the various recited diseases (emphysema, respiratory distress syndrome, pneumonia, pulmonary fibrosis, etc.) yields "unpredictable" results. First, it is not established that these diseases are exclusively, or even primarily, dependent on elastase. Numerous other enzymes are involved, as are various reactive oxygen species. Second, even if it is true that the symptoms of one of these diseases could be mitigated by administering one of the claimed compounds **before** the onset of symptoms, it would not follow therefrom that the diseases can be successfully treated if the compound is administered **after** the disease is firmly established, and tissue damage has become extensive. Accordingly, "undue experimentation" would be required to practice the claimed invention.

In response to the foregoing, applicants have simply restated a few of the examiner's observations, and have argued, in effect, that experiments conducted in vivo necessary provide enablement for treatment of diseases. However, applicants are not correct on this point. It is true that results obtained by observing the physiological consequences of administering a compound are <u>often</u> sufficient to enable a claim drawn to treatment of a specific disease, but *in vivo* data, in and of itself is by no means equivalent to a showing of how to "make and use" the compound in question. As a first step in the dialog, it would be

helpful if applicants would at least make an (unsubstantiated) assertion about which disease specifically, among those recited in the specification, can be successfully treated using a compound which is effective to reduce the amount of hemoglobin in the washing of a broncho-alveolar lavage. This is a critical first step in the dialog. If applicants cannot even make an assertion about which disease can be treated, there can be no argument that the specification teaches the skilled artisan how to treat the disease. In the event that applicants are willing to make such an assertion, the next question will be, to what extent is the experiment (described on pages 22-24) accepted by pulmonary specialists (or allergists) as being a suitable animal model of the disease in question? As indicated above, one of the "Forman factors" is the "state of the prior art". The examiner asserts that, at the time of the invention, there was no recognition among pulmonary specialists or allergists that the experiment described on pages 22-24 (specification) is indicative or predictive of a successful treatment of emphysema, RDS, cystic pulmonary fibrosis, or any of the other recited diseases. Given the absence of guidance as to which disease can be successfully treated, and the complete absence of any reason to expect a correlation between the observed reduction of hemoglobin content in broncho-alveolar lavages, and the successful treatment of a human disease, the skilled artisan would conclude that "undue experimentation" would be required to use the claimed compounds to treat human disease.

It is suggested that the term "pharmaceutical" be deleted.

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Claim 9 is rejected under 35 U.S.C. 112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 makes reference to human neutro**phil**ic elastase. However, this appears to be an error. The correct term is *neutrophil*, rather than "neutrophilic"

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at 571-272-0951. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

D. Lukton

DAVID LUKTON
PATENT EXAMINER
GROUP 1600